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Meta-analysis of the prevalence of renal cancer detected by abdominal ultrasonography

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Background: The potential for an ultrasound-based screening programme for renal cell carcinoma (RCC) to improve survival through early detection has been the subject of much debate. The prevalence of ultrasound-detected asymptomatic RCC is an important first step to establishing whether a screening programme may be feasible.

Methods: A systematic search of MEDLINE and Embase was performed up to March 2016 to identify studies reporting the prevalence of renal masses and RCC. Two populations of patients were chosen: asymptomatic individuals undergoing screening ultrasonography and patients undergoing ultrasonography for abdominal symptoms not related to RCC. A random-effects meta-analysis was performed. Study quality was evaluated using a validated eight-point checklist.

Results: Sixteen studies (413 551 patients) were included in the final analysis. The pooled prevalence of renal mass was 0.36 (95 per cent c.i. 0.23 to 0.52) per cent and the prevalence of histologically proven RCC was 0.10 (0.06 to 0.15) per cent. The prevalence of RCC was more than double in studies from Europe and North America than in those from Asia: 0.17 (0.09 to 0.27) *versus* 0.06 (0.03 to 0.09) per cent respectively. Data on 205 screen-detected RCCs showed that 84.4 per cent of tumours were stage T1–T2 N0, 13.7 per cent were T3–T4 N0, and only 2.0 per cent had positive nodes or metastases at diagnosis.

Conclusion: At least one RCC would be detected per 1000 individuals screened. The majority of tumours identified are early stage (T1–T2).

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Introduction

Overall survival from renal cell carcinoma (RCC) is poor, with a 5-year age-standardized relative survival rate of 47 per cent in the UK¹. Half of all patients with renal cancer present with asymptomatic disease and so many cancers are detected late, with over one-quarter of individuals diagnosed with RCC having evidence of metastases at presentation^{2,3}. Patients with metastases have a 5-year age-standardized relative survival rate of 6 per cent, compared with 84 per cent in patients with stage I disease¹. Incidentally detected tumours are generally smaller and are associated with improved survival relative

to symptomatic tumours, independent of tumour grade and stage^{4,5}.

A screening programme consisting of abdominal ultrasonography, potentially in a selected higher-risk population, in theory could improve survival outcomes through early detection and treatment of RCC. Previously, the low prevalence of renal cancer in the general population and relatively poorly understood natural history of renal masses were considered major barriers to establishing a cost-effective screening service⁶. More recently, there has been a resurgence in interest in a screening programme for RCC⁷. The established abdominal aortic aneurysm (AAA) screening programme in men over the age of 65 years in

the UK represents an ideal model to explore the possibility of screening for RCC as there are similarities in risk factors and mode of detection between RCC and AAA⁸. Furthermore, although a number of drugs for the treatment of metastatic RCC are available, they are very expensive^{9–11}. It has been postulated that early detection of asymptomatic RCC through a targeted national screening programme may potentially downstage the disease, reducing the prevalence of metastatic tumours and associated expenditure relating to systemic therapies.

Before consideration of a screening study for RCC, it is essential to assess potential cost-effectiveness, by assembling all relevant evidence on the incremental costs and consequences of screening into an economic model. One of the key parameters that will inform cost-effectiveness is the prevalence of renal masses and RCC in a screened population¹²; therefore, a systematic review and meta-analysis was performed to determine RCC prevalence.

Methods

Data sources and search strategy

The study protocol was registered on the PROSPERO database (<http://www.crd.york.ac.uk/PROSPERO/>; CRD 42016036899) and the study conducted in accordance with PRISMA guidelines¹³. A systematic literature search was performed in MEDLINE (January 1976 to March 2016) and Embase (January 1976 to March 2016) databases. Full details of the keywords and subject headings used are available in *Table S1* (supporting information). The reference lists of all relevant articles were reviewed manually.

Inclusion and exclusion criteria

Study inclusion, data extraction and data quality assessments were performed independently by two reviewers, with discrepancies resolved by a third investigator. Full inclusion and exclusion criteria are reported in *Table S2* (supporting information). Studies were included in the analysis if the prevalence of renal masses and/or RCC was reported in asymptomatic individuals undergoing abdominal ultrasonography (screening group), patients undergoing abdominal ultrasonography for a medical reason not related to RCC (incidental finding group) or the study comprised a combination of both screened as well as non-screened individuals (mixed group). Studies were excluded if ultrasound imaging was performed in individuals who did not represent a general adult population or if patients had symptoms of renal cancer (flank

pain, abdominal mass, non-visible and/or visible haematuria). Patients undergoing ultrasonography for suspected renal colic were also excluded as symptoms may have been secondary to RCC rather than renal stones. Studies that undertook ultrasound screening in individuals with familial syndromes predisposing to RCC, or patients with renal transplant or end-stage renal disease were also excluded from the analysis.

Study quality assessment

A validated checklist was used to assess the quality of studies reporting the prevalence of renal masses in a screening population, with studies scored out of a total of 8 points¹⁴. Item 6 on the checklist evaluates whether the studies reported the participation rate of individuals invited to attend screening. Studies reporting the prevalence of incidental renal masses in patients undergoing ultrasonography for a non-urological complaint were assessed on a modified 7-point checklist, as item 6 was no longer a valid item in this group. Item 3 on the checklist evaluates whether the study sample size was sufficient to estimate prevalence with an adequate level of confidence and precision. Studies were awarded a point if they included more than 5107 participants (*Appendix S1*, supporting information)^{15,16}. Study quality was used to perform subgroup analysis. No studies were excluded from the meta-analysis based on quality score or sample size.

Study outcomes

The primary study outcomes were the prevalence of solid or complex cystic renal masses suspicious for RCC on ultrasonography, and the prevalence and stage distribution of histologically proven RCC in asymptomatic individuals. The secondary outcome was the prevalence of other renal and adrenal pathology. Preplanned subgroup analysis consisted of study type (screening, mixed or incidental finding), study geographical region of origin, publication year and study quality. The prevalence of RCC by established risk factors such as age, sex, hypertension, smoking and BMI was assessed.

Statistical analysis

The meta-analysis was performed on the double arcsine transformation (*Appendix S2*, supporting information)¹⁷ for each proportion, using the generic inverse-variance method. The double arcsine transformation stabilizes the variance and is particularly useful for proportions that are at the extremes of the 0 to 1 range, as is the

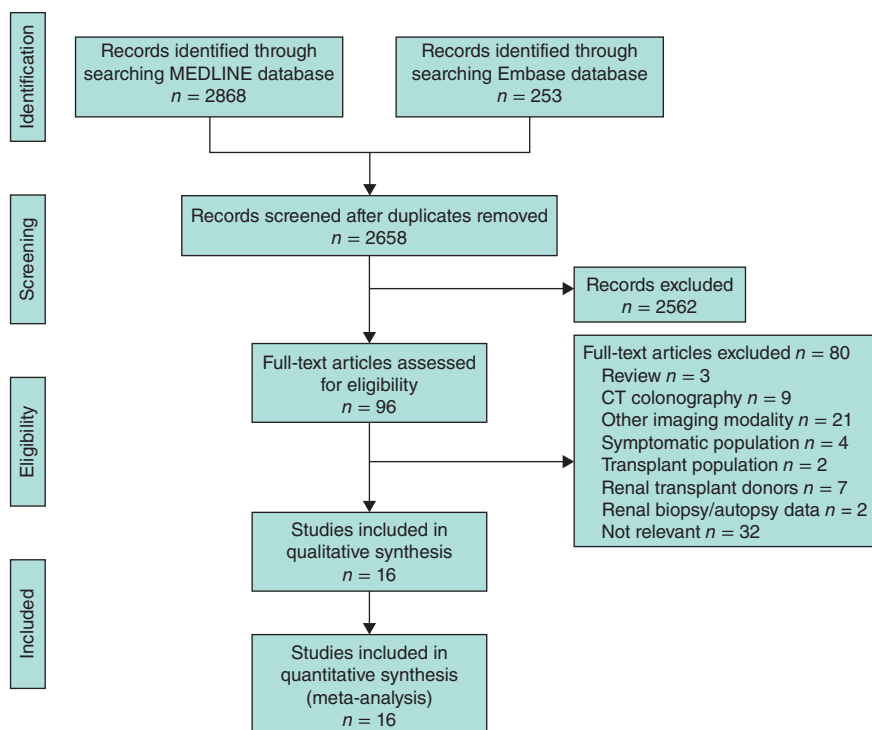


Fig. 1 PRISMA flow diagram showing search strategy

case for an uncommon condition such as RCC¹⁷. In this case, asymmetrical confidence intervals are created to avoid reporting a prevalence in the negative range. As such, it is not appropriate to use funnel plots to assess for publication bias, as the typical funnel shape relies on symmetry of confidence intervals. Heterogeneity was assessed using the χ^2 test and the I^2 (Cochran's Q) statistic. The pooled prevalence was calculated using a random-effects model as there was significant heterogeneity between studies. Meta-regression was used to assess the association between study characteristics (study type, size, publication year and geographical region) and the prevalence of RCC. $P < 0.050$ was considered statistically significant. The statistical analysis was performed using Stata[®] version 12.0 (Stata Corp, College Station, Texas, USA).

Results

Data retrieval and study quality

Following exclusion of duplicates, the search yielded 2658 articles. Sixteen studies were included in the final meta-analysis for renal masses (413 551 individuals) (Fig. 1 and Table 1)^{8,16,18–31}. The median quality score for studies in the screening and mixed groups was 4 (range 3–6) of 8, whereas studies in the non-screening group only achieved

a median score of 1.5 (range 1–3) of 7 (Table S3, supporting information). All studies were observational, consisting of one study arm alone (no non-screening comparator), and none used a random sampling method. Only one study²² commented on the participation rate of individuals invited to attend screening. None of the studies reported 95 per cent confidence intervals for point estimates of prevalence, despite the fact that this was an item on the quality assessment checklist (although this is readily calculable, given knowledge of the sample size). Three studies^{16,26,30} did not clearly state ultrasound criteria used to define a suspicious renal mass and three^{21,25,29} further studies included only solid (rather than complex cystic) masses in this definition. Five studies^{23,26–29} reported data on the prevalence of renal masses, but no histological data were available, so these studies were excluded from the analysis of the prevalence of histologically proven RCC. All studies reporting the prevalence of histologically proven RCC were based on operative (rather than biopsy) specimens.

Primary outcomes

The pooled prevalence of renal masses was 0.36 (95 per cent c.i. 0.23 to 0.52) per cent (Fig. 2) and that of histologically proven RCC was 0.10 (0.06 to 0.15) per cent (Fig. 3).

Table 1 Characteristics of included studies

Reference	Country	Data collection dates	Sample size	Sample recruitment	Age (years)*	Male sex (%)
Fujii <i>et al.</i> ¹⁸	Japan	April 1985 to March 1991	17 941	Asymptomatic individuals, employee health check-up	53 (21–85)†	72
Spouge <i>et al.</i> ¹⁹	Canada	6-month interval, not specified	1000	Asymptomatic individuals, employee health check-up for business executives	46.2 (29–63)	91
Spouge <i>et al.</i> ¹⁹ (2)	Canada	2.5-year interval, not specified	7925	Asymptomatic individuals, employee health check-up for business executives	n.r.	n.r.
Mihara <i>et al.</i> ¹⁶	Japan	August 1983 to March 1996	219 640	Asymptomatic screening of general population	(29–70)	n.r.
Tsuboi <i>et al.</i> ²⁰	Japan	January 1993 to June 1997	60 604	Asymptomatic individuals, health check-up for general population	(15–96)	67
Mizuma <i>et al.</i> ²¹	Japan	February 1990 to December 1995	16 024	Asymptomatic individuals, health check-up for general population	47 (25–84)	58
Filipas <i>et al.</i> ²²	Germany	December 1996 for 13 months and January 1998 for 13 months	9959	Asymptomatic screening of general population, individuals aged > 40 years	61 (40–94)	49
Malaeb <i>et al.</i> ⁸	USA	1993 to 1997	6678	Asymptomatic screening of veterans (in conjunction with AAA screening)	66.2 (50–79)	97
Mosharafa ²³	8 Middle Eastern countries	January 2005 to December 2005	8551	Asymptomatic individuals, health check-up for general population	43.5(13.9)‡	70
Tosaka <i>et al.</i> ²⁴	Japan	1982 to 1988	41 364 (20 897 screening, 20 467 non-screening)	Mixed: asymptomatic individuals (part of health check-up) and patients undergoing abdominal ultrasonography for non-urolological complaint	n.r.	n.r.
Haliloglu <i>et al.</i> ²⁵	Turkey	March 1995 to February 2008	18 203	Mixed: asymptomatic individuals (part of health check-up) and patients having ultrasound for LUTS	55 (33–90)	64
Fields and Calvert-Hill ²⁶	USA	n.r.	500	Abdominal ultrasonography for non-urolological complaint	n.r.	n.r.
Bodner <i>et al.</i> ²⁷	USA	n.r.	86	Patients with spinal cord injury, no urological symptoms	41.7	99
Al-Durazi <i>et al.</i> ²⁸	Bahrain	January 2001 to December 2001	100	Men with acute retention secondary to BPH	67 (54–96)	100
Belani <i>et al.</i> ²⁹	USA	3 months, not specified	600	Abdominal ultrasonography for non-urolological complaint	53 (18–95)	32
Heikkinen <i>et al.</i> ³⁰	Finland	January 1993 to January 1994	400	Patients undergoing investigations for dyspepsia	Endoscopy-negative: 55.8 Endoscopy-positive: 58.3	38
Patel <i>et al.</i> ³¹	UK	April 1994 to February 2007	3976	Men with LUTS	65 (15–91)	100

*Values are mean (range) unless indicated otherwise; values are †median (range) and ‡mean(s.d.). n.r., Not reported; AAA, abdominal aortic aneurysm; LUTS, lower urinary tract symptoms; BPH, benign prostatic hyperplasia.

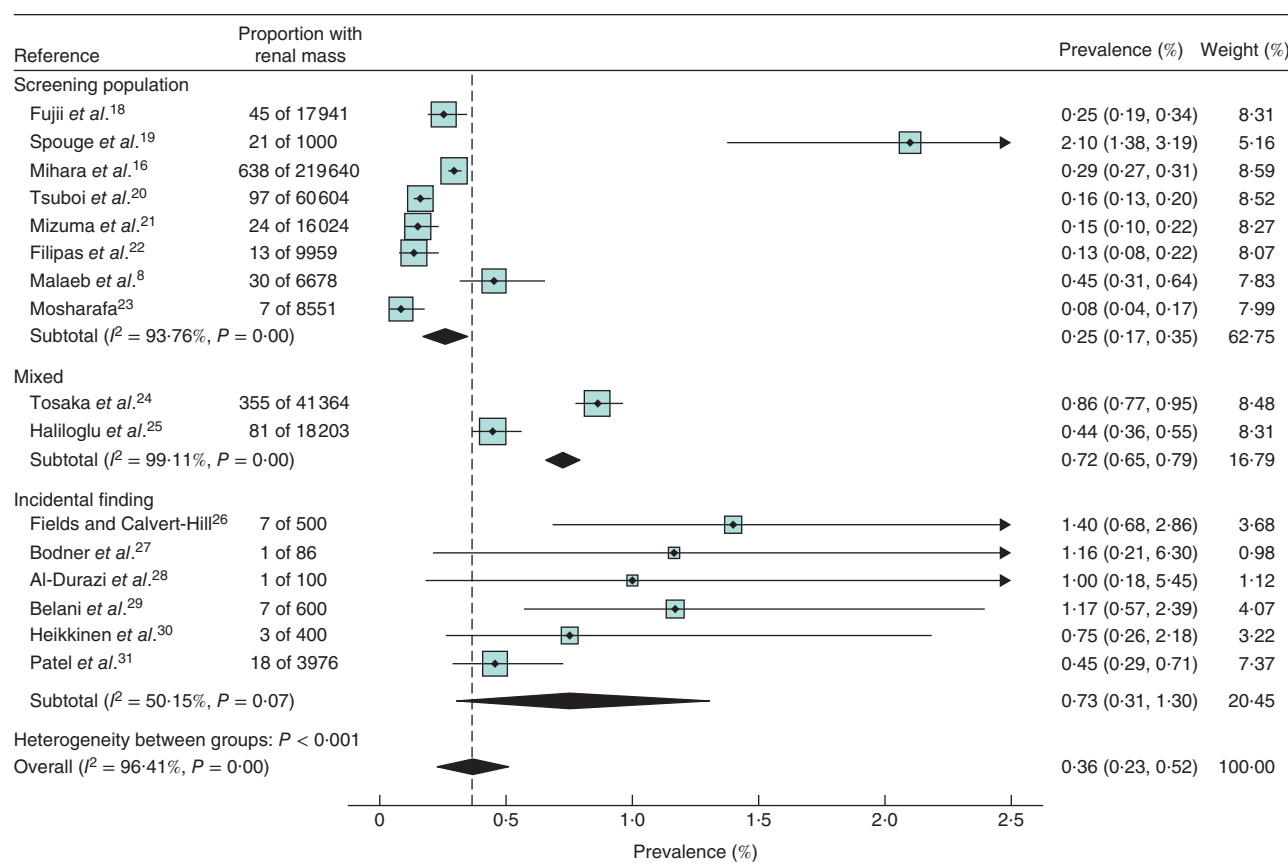


Fig. 2 Forest plot demonstrating the pooled prevalence of suspicious renal masses detected by ultrasonography, generated by a random-effects meta-analysis, for three subgroups: screening population, incidental finding and mixed. Prevalence is shown with 95 per cent confidence intervals

Significant study heterogeneity was noted for both outcomes ($\chi^2 = 327.60$, 15 d.f., $P < 0.001$, $I^2 = 96$ per cent and $\chi^2 = 112.62$, 11 d.f., $P < 0.001$, $I^2 = 91$ per cent).

Of the 11 studies investigating the prevalence of screen-detected RCC, a wide variation in the method used for reporting the size and stage of the tumours was noted. Only three studies^{8,16,22} reported data on the TNM staging of the detected RCCs; two of these used the TNM 1992 classification³² and one used TNM 1997³³. Two studies^{19,24} reported staging by Robson's classification³⁴ and three studies^{20,21,25} reported individual tumour size but not tumour stage. Differences in reporting of data limited the ability to pool results on the size and stage of screen-detected RCC, and so three different grouping methods were used (Table S4, supporting information). Data on 66 cancers from four studies^{8,21,22,25} were pooled to reveal that 45 per cent of screen-detected cancers were 4 cm or smaller in size, 41 per cent RCCs were between 4 and 7 cm, and only 14 per cent larger than 7 cm. Similarly, data

on 185 screen-detected RCCs from two further studies^{16,20} demonstrated that 80.0 per cent of tumours were 5 cm or smaller in size. Pooling data on 205 screen-detected RCCs from three studies^{8,16,22} showed that 84.4 per cent of tumours were category T1–T2 N0, 13.7 per cent were T3–T4 N0, and only 2.0 per cent had positive lymph nodes or metastases at diagnosis (TNM 1992 classification)³².

Secondary outcomes

A number of additional renal and adrenal pathologies were identified among the studies (Table S5, supporting information). Of note, Mihara and colleagues¹⁶ reported detection of an additional five (prevalence 0.002 per cent) malignant, non-RCC kidney lesions in addition to the RCCs (prevalence 0.086 per cent). Owing to heterogeneity of reported data, only the prevalence of asymptomatic hydronephrosis and renal stones were pooled in a meta-analysis. The pooled prevalence of hydronephrosis was 0.48 (0.21 to 0.87) per cent ($\chi^2 = 76.75$, 5 d.f., $P < 0.001$, $I^2 = 95$ per

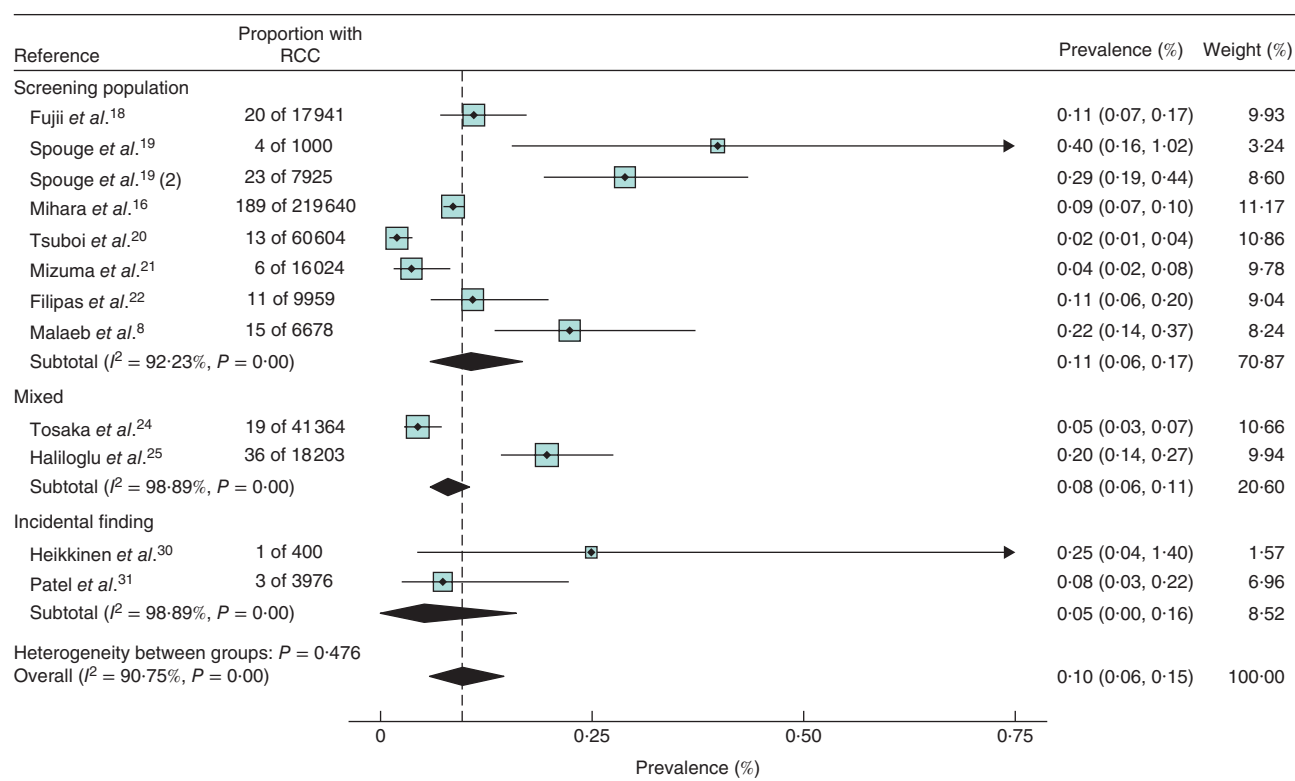


Fig. 3 Forest plot demonstrating the pooled prevalence of histologically proven renal cell carcinoma (RCC) detected by ultrasonography, generated by a random-effects meta-analysis, for three subgroups: screening population, incidental finding and mixed. Prevalence is shown with 95 per cent confidence intervals

Table 2 Subgroup analysis for the pooled prevalence of renal masses and histologically proven renal cell carcinoma

	Prevalence of renal masses (%)	Prevalence of histologically proven RCC (%)
Overall pooled prevalence	0.36 (0.23, 0.52)	0.10 (0.06, 0.15)
Study publication year		
Before 1999	0.67 (0.31, 1.13)	0.11 (0.06, 0.18)
2000 and 2004	0.17 (0.07, 0.30)	0.08 (0.02, 0.17)
2005 to present	0.32 (0.10, 0.67)	0.12 (0.04, 0.23)
Study quality		
Quality score ≥ 4	0.28 (0.19, 0.40)	0.12 (0.07, 0.18)
Quality score < 4	0.55 (0.22, 0.99)	0.03 (0.00, 0.09)
Geographical region		
Asia	0.30 (0.14, 0.52)	0.06 (0.03, 0.09)
Europe and North America	0.70 (0.31, 1.22)	0.17 (0.09, 0.27)
Middle East	0.16 (0.00, 0.66)	0.20 (0.14, 0.27)

Values in parentheses are 95 per cent confidence intervals. RCC, renal cell carcinoma.

cent) (Fig. S1, supporting information) and the prevalence of asymptomatic renal stones was 1.82 (0.59 to 3.64) per cent ($\chi^2 = 844.78$, 9 d.f., $P < 0.001$, $I^2 = 100$ per cent) (Fig. S2, supporting information).

Subgroup analyses

The geographical region in which the study was undertaken was the only subgroup that consistently affected the prevalence of renal masses and histologically proven RCC (Table 2). However, assessing the prevalence by study geographical region did not reduce heterogeneity. The prevalence of renal masses and RCC in studies from Europe and North America was more than double that in studies from Asia (renal mass: 0.70 (95 per cent c.i. 0.31 to 1.22) *versus* 0.30 (0.14 to 0.52) per cent respectively; RCC 0.17 (0.09 to 0.27) *versus* 0.06 (0.03 to 0.09) per cent). Geographical region was a significant determinant of the prevalence of RCC in meta-regression ($P = 0.002$), but study type and quality were not ($P = 0.876$ and $P = 0.432$ respectively) (Table S6, supporting information). The effect of publication year, study type and study quality was not consistent across the two outcomes.

The pooled prevalence of renal masses was higher in the non-screening subgroup than the screening subgroup (0.73 (0.31 to 1.30) *versus* 0.25 (0.17 to 0.35) per cent respectively) (Fig. 2); however, this pattern was not noted in terms of the prevalence of RCC, which was lower in

the non-screening compared with the screening subgroup (0.05 (0.00 to 0.16) *versus* 0.11 (0.06 to 0.17) per cent).

There were insufficient data to assess the impact of established risk factors on the development of RCC, including patient age, hypertension, smoking status and BMI. Only five studies^{8,18,20–22} reported sufficient data to allow calculation of the prevalence of RCC by sex. The pooled prevalence was higher in men than women (0.09 (0.03 to 0.18) *versus* 0.01 (0.00 to 0.05) per cent).

Discussion

Early detection and screening for cancer has been identified as a key priority for the National Health Service, with increased resource allocation and media coverage³⁵. Although the UK National Screening Committee has released recommendations regarding screening for colorectal, breast, prostate, ovarian and lung cancer, screening for RCC has yet to be discussed as there are currently incomplete data, with relatively little research published in the literature over the past decade^{2,36}. Data on the prevalence of RCC in asymptomatic individuals undergoing abdominal ultrasonography are lacking, but are essential to inform an economic evaluation of the cost-effectiveness of an ultrasound-based screening programme. Here, a pooled prevalence of renal masses was 0.36 (95 per cent c.i. 0.23 to 0.52) per cent, with a pooled prevalence of histologically proven RCC of 0.10 (0.06 to 0.15) per cent. Current National Cancer Intelligence Network data³⁷ suggest that, although 44 per cent of patients diagnosed with RCC have stage disease I at presentation, only 10 per cent have stage II tumours, with over 25 per cent having metastases. The present meta-analysis showed that 84.4 per cent of screen-detected tumours were stage T1–T2N0, 13.7 per cent were T3–T4N0, and only 2.0 per cent had positive nodes or metastases at diagnosis, suggesting a potential favourable stage shift in screen-detected disease.

It is anticipated that focused screening renal ultrasonography will lead to detection of other benign and malignant renal and adrenal abnormalities. The prevalence of screen-detected hydronephrosis was estimated to be 0.48 (0.21 to 0.87) per cent and that of renal stones 1.82 (0.59 to 3.64 per cent). Unfortunately, there were insufficient data to estimate the pooled prevalence of benign masses of the renal fossa, such as angiomyolipoma and oncocytoma, or the prevalence of renal cysts, the most common screen-detected renal pathology. The prevalence of asymptomatic cysts is estimated to be 30 per cent in individuals aged over 70 years³⁸. A proportion of screen-detected cysts may require further imaging, discussion with a specialist and, potentially, treatment.

An evaluation of a screening programme for RCC must take into consideration the impact of incidentally detected benign renal lesions on patients and health services. There is a potential for false-positive results and overdiagnosis of slow-growing small renal masses (SRM). Currently, 15–30 per cent of SRM are found to be benign following surgical excision^{39–41}. Advances in determination of the aetiology of SRM, with increased use and better interpretation of renal biopsy, may reduce these rates in future⁴². Up to one-third of small renal cancers exhibit aggressive potential (rapid growth or doubling time less than 12 months), with the remainder growing slowly or remaining stable in size^{43,44}. It is anticipated that, in future, the development of non-invasive modalities, such as measurement of urinary biomarkers, will allow improved discrimination between benign and malignant SRM (with further differentiation between indolent and aggressive RCC), enabling personalized treatment strategies and reducing overtreatment⁴⁵. These considerations may be offset further by the potential benefit derived from early detection of other malignancies within the renal fossa (including adrenal and upper urinary tract urothelial cell cancers, renal secondary metastases, renal carcinoid, sarcoma and lymphoma). Spouge and colleagues¹⁹ reported the prevalence of these combined malignancies as 0.2 per cent, whereas Mizuma *et al.*²¹, Malaeb and colleagues⁸ and Patel and co-workers³¹ all reported a prevalence of 0.03 per cent. These rates vary considerably, and insufficient data were available for meta-analysis. Further studies are needed to quantify this and to estimate the potential impact on health services.

It is likely that this meta-analysis underestimated the true prevalence of histologically proven RCC. Several studies^{8,16,20,22} reported a higher prevalence of suspected RCC; however, owing to patient loss to follow-up or contraindications to surgery, histological confirmation was only available in a portion of these. For example, Malaeb and colleagues⁸ screened 6678 individuals with ultrasonography and confirmatory CT demonstrated 22 solid renal masses suspicious for RCC; however, histology was available for only 15 of these, potentially underestimating the true prevalence of malignancy. Furthermore, only half of the studies included in the meta-analysis represented a European or North American population, with the remainder originating from Asia or the Middle East. The results suggest that there is significant variability between the prevalence of screen-detected RCC in different geographical areas, in keeping with known epidemiological data⁴⁶. The prevalence of RCC in studies originating from Europe and North America was more than double that in Asia. Another factor that may have contributed to a potential

underestimation of the true prevalence of RCC is the young age of the screening study participants. Only one of eight screening studies reported a participant mean age over 65 years and five studies included individuals aged less than 30 years. Young patients with RCC are at greater risk of familial syndromes predisposing to cancer; however, owing to lack of patient-level data, it was not possible to exclude young participants from the analysis by age. In addition, the included studies were published between 1985 and 2010, with over 13 of 16 published before 2006. Such factors restrict the applicability of these results to the population of interest in the UK, and highlight the need for more high-quality research in a contemporary Western population. Obesity and older age are established risk factors for the development of RCC^{47,48} and, with the growing obesity epidemic and ageing population, the incidence of RCC is expected to rise in the future.

This meta-analysis included relatively low-quality studies. The retrospective design and substantial rates of loss to follow-up should all be taken into consideration when interpreting the results. In addition, there were discrepancies in the ultrasound criteria used to define a renal mass in different studies. Importantly, none of the studies compared a screening intervention with a non-screening group or used a random sampling method to select study participants. In addition, methods used to recruit participants may also introduce bias within the screening group. For example, two studies^{18,19} offered abdominal ultrasonography to asymptomatic individuals as part of an employee health check-up, rather than screening individuals through a population registry. The inclusion of studies assessing the prevalence of renal cancer in patients undergoing abdominal ultrasound examination for a medical reason not related to kidney cancer (incidental finding group) may have introduced heterogeneity in the data. These smaller studies are also more prone to potential publication bias. However, neither study type nor quality score were found to be significant factors in meta-regression, and heterogeneity remained high even when only screening population studies were pooled. The persistent heterogeneity may in part be attributed to differences in study design and patient populations. The included studies reported only limited data on the prevalence of renal cancer by established risk factors, precluding any formal analysis. Although, as expected, the prevalence of RCC was found to be higher in male compared with female patients, it is likely the estimate of effect size is inaccurate owing to small sample sizes, hindering conclusions regarding the potential for targeted screening.

The results of this meta-analysis on the prevalence of RCC detected by ultrasonography are broadly in keeping

with what would be expected from the data published for screening using non-contrast CT. Two studies have attempted to pool data from the literature to quantify the prevalence of renal cancer in asymptomatic individuals, and both of these used non-contrast CT rather than ultrasound imaging as a screening tool. Fenton and Weiss⁴⁹ calculated the pooled prevalence of renal cancer in asymptomatic American patients undergoing non-contrast screening CT as 0.21 (95 per cent c.i. 0.14 to 0.28) per cent. Wernli *et al.*⁵⁰ estimated the pooled prevalence of renal masses as 0.22 per cent in patients undergoing non-contrast CT colonography, with a rate of 0.06 per cent in screened populations and 0.42 per cent in non-screening populations. Conversely, ultrasonography is known to be less sensitive and specific than non-contrast CT for the detection of renal cancers; ultrasound detection rates are dependent on renal lesion size, a factor that would need to be considered in the design of a screening programme in terms of frequency of ultrasonography⁵¹. Studies examining autopsies or cadaveric organ donors have estimated a prevalence of RCC of 0.7–0.9 per cent (mean age of study participants 65 years)^{52,53}. This is substantially higher than the prevalence suggested by the present meta-analysis, raising once again the possibility that the true prevalence of histologically proven RCC may have been underestimated.

This meta-analysis suggests that screening 1000 individuals would result in four patients undergoing further imaging of a renal mass, and that at least one of these patients would be diagnosed with RCC. The clinical significance of these findings is best appreciated in the context of other established screening programmes (*Fig. 4*). The NHS AAA screening programme identifies ten men with an AAA of 3 cm or larger for every 1000 individuals screened. However, only two men undergo elective surgery to repair a large AAA following initial screening⁵⁴. An additional six individuals require elective surgery to repair a large AAA following active surveillance over a 20-year interval⁵⁵. Results from the Bowel Cancer Screening Programme in England⁵⁶ have demonstrated that 1.6 colorectal cancers are detected for every 1000 individuals screened using guaiac-based faecal occult blood tests. An additional six cases are detected with high-risk adenomatous polyps requiring surveillance colonoscopy. The UK Breast Cancer Screening Programme⁵⁷ breast cancer detection rate is 8.3 per 1000 women screened. This number is much higher than the projected values for RCC screening; however, it is estimated that 15–25 per cent of screen-detected breast cancers are overdiagnosed⁵⁸. Screening for RCC may compare favourably with the established programmes for AAA and colorectal cancer, although intrinsic

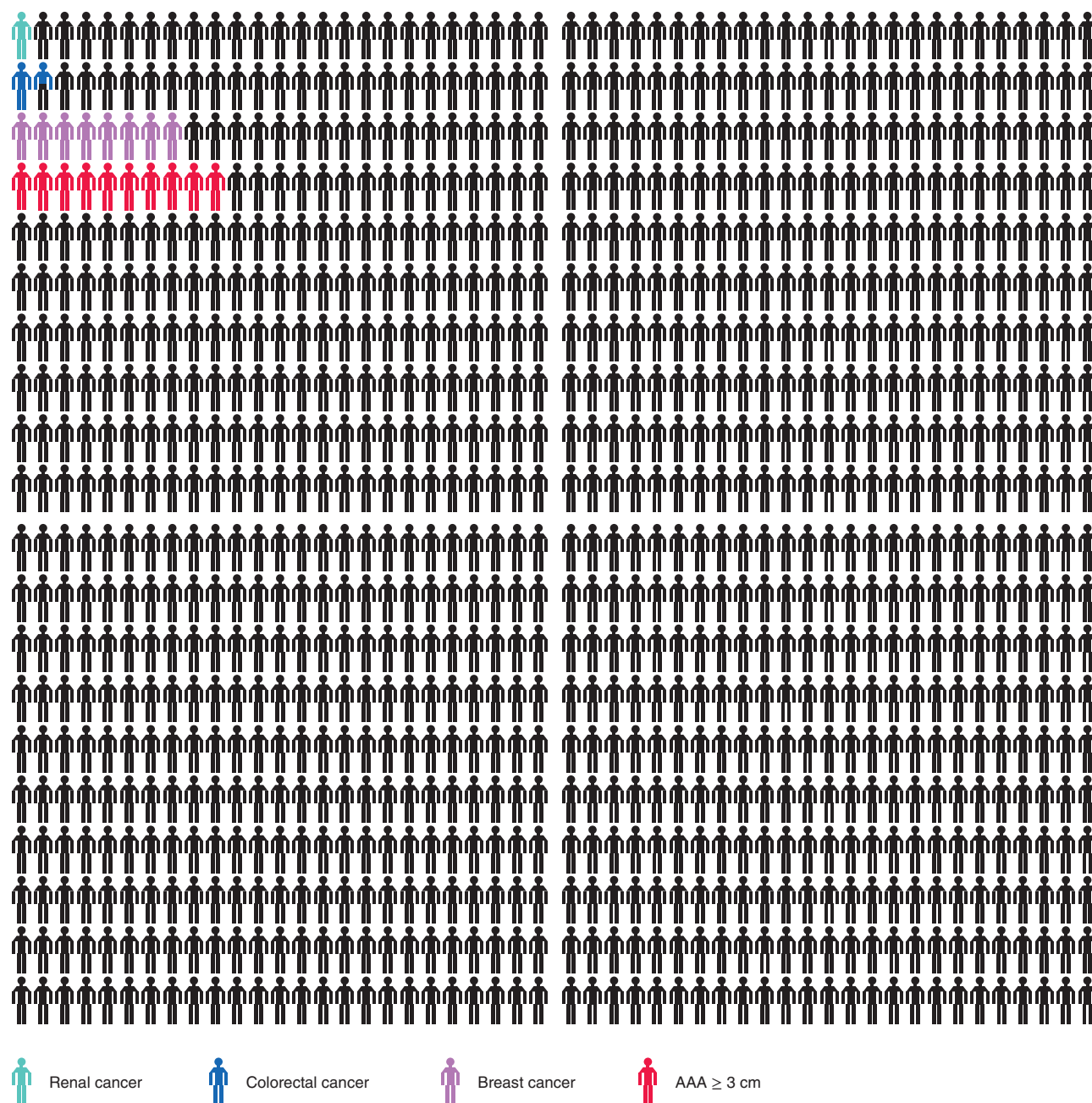


Fig. 4 Infographic delineating comparative detection ability of established UK screening programmes compared with screening for renal cell carcinoma. The present meta-analysis suggests that screening 1000 individuals would detect at least one renal cell carcinoma. Screening 1000 individuals detects 1.6 colorectal cancers, eight breast cancers and ten abdominal aortic aneurysms (AAAs) with a diameter of at least 3 cm

differences underlying each screening programme and the individual nature of each disease make direct comparisons artificial.

In isolation, this meta-analysis is insufficient to support or refute a screening programme for RCC and should

not replace a full consideration of the Wilson–Jungner criteria⁵⁹. A cost-effectiveness analysis is beyond the scope of this paper, but should constitute an essential next step towards establishing the potential value of screening.

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Supporting information

Additional supporting information may be found in the online version of this article:

Appendix S1 Sample size calculation for study quality assessment (Word document)

Appendix S2 Freeman–Tukey double arcsine transformation (Word document)

Table S1 Review search strategy (Word document)

Table S2 Inclusion and exclusion criteria (Word document)

Table S3 Assessment of methodological quality (Word document)

Table S4 Size and stage distribution of screen-detected renal cell carcinomas (Word document)

Table S5 Prevalence of renal and adrenal pathology (Word document)

Table S6 Meta-regression for prevalence of histologically proven renal cell carcinoma (Word document)

Fig. S1 Forest plot demonstrating the pooled prevalence of hydronephrosis detected by ultrasonography (Word document)

Fig. S2 Forest plot demonstrating the pooled prevalence of renal stones detected by ultrasonography (Word document)

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